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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,401	09/12/2005	Clifford Charles Shone	MSQ01-003-US	2849

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EVAN LAW GROUP LLC
600 WEST JACKSON BLVD., SUITE 625
CHICAGO, IL 60661

EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
04/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,401	SHONE ET AL.	
	Examiner	Art Unit	
	BRIAN GANGLE	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-72* is/are pending in the application.

4a) Of the above claim(s) *51,54,56,59-64,66 and 68-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52,53,55,57,58,65 and 67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/18/05,3/2/07,7/25/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Upon further consideration, Group IV (claims 65 and 67) is rejoined with Group II.

Applicant's election with traverse of Group II and the translocation domain from *C. botulinum* in the reply filed on 2/1/2008 is acknowledged. The traversal is on the ground(s) that the technical feature linking the groups is not simply a composition comprising a therapeutic agent which inhibits a Rho GTPase and a neuronal cell targeting component comprising an Hc domain of botulinum C1 toxin, as the examiner has asserted. Applicant argues that the botulinum toxin domain must be made recombinantly and argues that recombinantly made botulinum toxin has significantly reduced affinity and specificity for neuronal cells. Applicant argues that, because of these differences, the botulinum toxin described by Shone *et al.* does not anticipate the technical feature linking the inventions.

This is not found persuasive because the construct of Shone *et al.* is made recombinantly; therefore, whether there is a difference between recombinant botulinum toxins and natural botulinum toxins is immaterial (see page 6, line 26).

The requirement is still deemed proper and is therefore made FINAL.

Claims 51-72 are pending. Claims 51, 54, 56, 59-64, 66, and 68-72 are withdrawn as being drawn to non-elected inventions. Claims 52-53, 55, 57-58, 65, and 67 are currently under examination.

Information Disclosure Statement

The information disclosure statements filed on 1/18/2005, 3/2/2007, and 7/25/2007 have been considered. Initialed copies are enclosed.

Claim Objections

Claims 52-53, 55, 57-58, 65, and 67 are objected to because of the following informalities: the claims are dependent on a non-elected claim. Appropriate correction is required.

Claim 55 is objected to because of the following informalities: the claim makes reference to *C. botulinum*. Scientific names of organisms should be italicized. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 67 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 67 is rendered vague and indefinite by the use of the term "collagen-like spacer." This term is not defined in the specification. It is not clear what degree of similarity a molecule must have to collagen in order to be "collagen-like."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 52-53, 55, 57-58, 65, and 67 are rejected under 35 U.S.C. 102(b) as being anticipated by Shone *et al.* (PCT Publication WO 00/28041, 2000, IDS filed 1/18/2005).

The instant claims are drawn to compositions for delivery of a therapeutic agent to a neuronal cell, comprising a therapeutic agent which inhibits at least one member of the Rho group of GTPases; a neuronal cell targeting component which comprises a Hc domain of botulinum C1 toxin or a fragment thereof which retains the function of the native Hc domain, wherein the Hc domain has been made recombinantly; and a domain for translocation of the therapeutic agent into a cell, wherein the translocation domain comprises botulinum C1 toxin and fragments thereof (claims 52, 53, 55, and 57). The translocation domain is required to be a membrane disrupting peptide (which botulinum C1 toxin is) (claim 58). Further dependent claims limit the composition to wherein the therapeutic agent, the Hc domain and the

translocation domain are joined to each other directly or via a linker molecule (claim 65) and where the linker molecule is selected from the group consisting of the interdomain linker of cellulase, collagen-like spacer, trypsin-sensitive diphtheria toxin peptide, and linker molecules having an amino acid sequence of SEQ ID Nos: 16-27 (claim 67).

Shone *et al.* disclose a composition for delivery of superoxide dismutase linked to a neuronal cell targeting component that comprises a first domain that binds to a neuronal cell and a second domain that translocates the superoxide dismutase into the neuronal cell (see abstract). As evidenced by Heo *et al.* (J. Biol. Chem., 280:31003-31010, 2005) superoxide dismutase abolishes Rac1 guanine nucleotide dissociation; therefore it inhibits a Rho GTPase (page 31004, column 2, paragraph 1). Shone *et al.* disclose that their construct is made recombinantly (page 6, line 26). Shone *et al.* describes the binding domain and the translocation domain as coming from a clostridial neurotoxin, including serotype C1 (page 12, line 23 through page 14, line 15). Shone *et al.* also disclose the use of a linker molecule between the therapeutic agent and the toxin, where the linker is a peptide with the sequence CGLVPAGSP, which corresponds to SEQ ID NO:23 of the instant application (page 10, lines 20-23).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRIAN GANGLE whose telephone number is (571)272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/BRIAN GANGLE/
Examiner, Art Unit 1645

/Shanon A. Foley/
Supervisory Patent Examiner, Art Unit 1645